

**WE CLAIM:**

1. A method for preparing a positively charged compound-containing matrix useful for delivery of a positively charged compound to a mammalian subject, comprising:
  - (a) providing a first crosslinkable component having  $m$  nucleophilic groups, wherein  $m \geq 2$ ;
  - (b) providing a second crosslinkable component having  $n$  electrophilic groups capable of reaction with the  $m$  nucleophilic groups to form covalent bonds, wherein  $n \geq 2$  and  $m + n \geq 5$ ;
  - (c) admixing the first and second crosslinkable components in a basic, aqueous medium to initiate crosslinking and form a crosslinked matrix with an excess of negatively charged electrophilic groups; and
  - (d) contacting the negatively charged crosslinked matrix with the positively charged compound to allow ionic binding therebetween,  
wherein the first and second crosslinkable components are biocompatible, synthetic, and nonimmunogenic.
2. The method of claim 1, wherein the  $m$  nucleophilic groups in the first crosslinkable component are identical.
3. The method of claim 1, wherein at least two of the  $m$  nucleophilic groups in the first crosslinkable component are different.
4. The method of claim 1, wherein the  $n$  electrophilic groups in the second crosslinkable component are identical.
5. The method of claim 2, wherein the  $n$  electrophilic groups in the second crosslinkable component are identical.
6. The method of claim 3, wherein the  $n$  electrophilic groups in the second crosslinkable component are identical.
7. The method of claim 1, wherein the  $n$  electrophilic groups in the second crosslinkable component are different.

8. The method of claim 2, wherein at least two of the n electrophilic groups in the second crosslinkable component are different.

9. The method of claim 3, wherein at least two of the n electrophilic groups in the second crosslinkable component are different.

10. The method of claim 1, wherein the m nucleophilic groups are bound to the first crosslinkable component through linking groups.

11. The method of claim 1, wherein the n nucleophilic groups are bound to the second crosslinkable component through linking groups.

12. The method of claim 1, wherein at least one of the first and second crosslinkable components is comprised of a hydrophilic polymer.

13. The method of claim 1, wherein at least one of the first and second crosslinkable components is comprised of a hydrophobic polymer.

14. The method of claim 1, wherein the m nucleophilic groups are primary amino groups.

15. The method of claim 14, wherein the first crosslinkable component is C<sub>2</sub>-C<sub>6</sub> hydrocarbyl substituted with amino groups.

16. The method of claim 14, wherein the first crosslinkable component is a secondary or tertiary amine NR<sub>1</sub>R<sub>2</sub>R<sub>3</sub> wherein R<sub>1</sub> is hydrogen or an amino-substituted lower alkyl group, and R<sub>2</sub> and R<sub>3</sub> are amino-substituted lower alkyl groups.

17. The method of claim 14, wherein the n electrophilic groups are selected from the group consisting of succinimidyl ester, sulfosuccinimidyl ester, maleimido, epoxy, isocyanato, thioisocyanato, and ethenesulfonyl.

18. The method of claim 17, wherein the n electrophilic groups are selected from the group consisting of succinimidyl ester and sulfosuccinimidyl ester.

19. The method of claim 1, wherein the m nucleophilic groups are sulfhydryl groups.
20. The method of claim 19, wherein the n electrophilic groups are sulfhydryl-reactive groups selected so as to form a thioester, thioether, or disulfide linkage upon reaction with the sulfhydryl groups.
21. The method of claim 1, wherein n=2.
22. The method of claim 1, wherein m=2.
23. The method of claim 1, wherein the crosslinking conditions comprise admixture in an aqueous medium.
24. The method of claim 23, wherein the first and second crosslinkable components each represent about 0.5 wt.% to about 20 wt.% of the composition formed upon admixture.
25. The method of claim 23, wherein the crosslinking conditions further comprise admixture at a pH in the range of 7 to 8.
26. The method of claim 25, wherein the first and second crosslinkable components are at concentrations of 20 mg/mL to 200 mg/mL of the composition formed upon admixture.
27. The method of claim 1, wherein the first crosslinkable component is in an aqueous solution, the second crosslinkable component is in dry, particulate form, and admixing comprises combining the second crosslinkable component with the aqueous solution of the first crosslinkable component.
28. The method of claim 27, wherein the first and second crosslinkable components each represent about 0.5 wt.% to about 20 wt.% of the composition formed upon admixture.
29. The method of claim 27, wherein the crosslinking conditions further comprise admixture at a pH in the range of 7 to 8.

30. The method of claim 29, wherein the first and second crosslinkable components are at concentrations of 20 mg/mL to 200 mg/mL of the composition formed upon admixture.
31. The method of claim 1, wherein the first crosslinkable component is present in a molar excess relative to the second crosslinkable component.
32. The method of claim 1, wherein the second crosslinkable component is present in a molar excess relative to the first crosslinkable component.
33. A positively charged compound-containing matrix prepared by the method of claim 1.